

CHAV 3.0-032PCT/US

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of  
LEONARD MACKLES

Serial No. 10/526,386

371 date: 02/28/2005

For: Dri Nasal Sprays

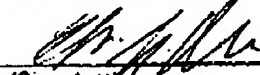
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Onni M. Behr 11/28/06Declaration

Leonard Mackles declares and says that:

1. He is the named inventor in the above identified application.
2. He holds the degree of B.S from Long Island University granted in 1951
3. For the past 50 years he has devoted his professional activities to creating novel formulations, particularly in the broadly defined area of health care and has been named as inventor or co inventor in numerous US and foreign patents.
4. He, or persons under his direct control and instruction has/have conducted certain experiments changing the order of preparation where the water soluble drugs such as Oxymetazoline HCl, the Glycol and the lactate esters are combined in different orders.
5. The experiments mentioned above are set forth below:

Example #1 12 Hour Duration Nasal Spray

	%
1. Oxymetazoline HCl	0.05
2. Propylene Glycol	3.00
3. C <sub>12</sub> -C <sub>18</sub> Alkyl Lactate	20.00
4. Caprylic/Capric Triglyceride (Neobee M-5)	76.95
	100.00

Method of Addition:

- 1.) Heat #'s 1 and 2 to 50°C. When dissolved, remove from heat.
- 2.) Add #3 to the batch and mix until clear and uniform.
- 3.) Add #4 to the batch and mix until clear and uniform.

The resultant nasal spray is clear, uniform and stable. It has no odor or taste and is non-irritating.

**Example #2** Oxymetazoline added last

	%
1. Oxymetazoline HCl	0.05
2. Propylene Glycol	3.00
3. C <sub>11</sub> -C <sub>13</sub> Alkyl Lactate	20.00
4. Caprylic/Capric Triglyceride (Neobee M-5)	<u>76.95</u>
	100.00

Method of Addition:

- 1.) Heat #'s 2, 3 and 4 to 50°C. Mix until clear and uniform.
- 2.) Add #1 to the batch and mix for 2 hours.

**Result:** The Oxymetazoline HCl did not dissolve. It settled on the bottom of the mixture. It did not go into solution after standing overnight.

**Example #3** 8 Hour Duration Nasal Spray

	%
1. Xylometazoline HCl	0.05
2. Propylene Glycol	3.00
3. C <sub>12</sub> -C <sub>13</sub> Alkyl Lactate	20.00
4. Propylene Glycol/Dicaprylic/Dicaprate (Neobee M-20)	<u>76.95</u>
	100.00

Method of Addition:

- 1.) Heat #'s 1 and 2 to 50°C. Mix the batch until it is clear and uniform.
- 2.) Add #3 to the batch and mix until clear and uniform.
- 3.) Add #4 to the batch and mix until clear and uniform.

The resultant nasal spray is clear, uniform and stable. It has no odor or taste and is non-irritating.

**Example #4:**

	%
1. Xylometazoline HCl	0.05
2. Propylene Glycol	3.00
3. C <sub>12</sub> -C <sub>13</sub> Alkyl Lactate	20.00
4. Propylene Glycol/Dicaprylic/Dicaprate (Neobee M-20)	<u>76.95</u>
	100.00

Method of Addition:

- 1.) Heat #'s 2, 3 and 4 to 50°C. Mix the batch until it is uniform.
- 2.) Add #1 to the batch and mix for 2 hours.

**Result:** The Xylometazoline HCl did not dissolve. It settled on the bottom of the mixture. It did not go into solution after standing overnight.

6. The reason the sequential addition system works while the total solvent system method does not is based on the specific solubilities of each component.
7. The water soluble drugs, Oxymetazoline HCl and Xylometazoline HCl are also soluble in Propylene Glycol or a similar glycol.
8. In turn the Propylene Glycol containing the drug is also soluble in lactate esters. The drug itself is not soluble in the lactate esters.
9. The three components are carried into the medium chain diglyceride and triglyceride carrier and remain soluble and stable.
10. These experiments clearly show that the order of addition is critical to the provision of a clear and useful solution.
11. Since a minimum of 4 components are required to be mixed there are  $1 \times 2 \times 3 \times 4$  possible combinations of order i.e. 24 possible combinations of order. To say that this number of experiments is what might be expected to be performed by one skilled in the art is quite unreasonable. The criticality of the order of mixing has thus been shown.
12. Furthermore as one skilled in the art, he states it as his opinion that the result he obtained would not have been obvious to anyone skilled in this art.
13. All statements made herein of his own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under 18 USC 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Further Declarant says not:



Leonard Mackles

Dated: 28 Nov 06

This is to certify that the foregoing paper is transmitted by telefax to the Commissioner for Patents at 571 273 8300 on

  
Omri M. Behr

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